

Extra-gonadal Germ Cell Tumour – What About the Testis!

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Abstract

Extra-gonadal germ cell tumours (EGGCT) are rare. Therefore further investigations of the testis is aimed at sourcing a possible primary origin of gonadal tumour. Over the years, various case series on EGGCT have been reported questioning its true nature as in a majority of them, a primary source is found in the testis, thus representing a metastatic gonadal tumour. The testis pathology could be either a true germ cell foci, an intra-tubular epithelial neoplasia or an area of fibrosis, indicating a 'burnt out tumour'. We report a 39-year-old male who underwent laparotomy and excision of a retroperitoneal tumour. Histopathological examination revealed retroperitoneal lymph node of mixed germ cell tumour origin. Clinical and ultrasound examination of bilateral testis was normal. The patient refused orchidectomy or a testicular biopsy. He underwent four cycles of bleomycin, cisplatin, and etoposide with no evidence of tumour recurrence on follow up and remains disease free after 12 months of diagnosis. A literature review of EGGCT, its relation and factors relating with future testicular tumour is presented.

Keywords: Extragonadal, germ cell tumour, testis, factors, histopathology, treatment

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Introduction

Extra-gonadal germ cell tumour (EGGCT) is a rare entity. Many researchers have questioned its true existence as a primary testicular lesions are often found via thorough investigations in cases presumed EGGCT. Controversies regarding subsequent management of the testis in cases of EGGCT are on-going as there are no clear set guidelines. Here, we report a case of a young man with EGGCT and look into literature with regards to current methods of the testis and follow up periods.

Case report

A 42-year-old man presented with lassitude for 1 month associated with low grade fever and intermittent back pain. He complained of loss of appetite for 3 weeks without obvious loss of weight.

Physical examination of the abdomen was unremarkable and there were no abnormalities of the external genitalia. A biochemical test offered by a private laboratory which included tumour markers revealed that his alpha-feto protein levels was 3238 ng/ml (0- 6.67ng/ml) beta-human chorionic gonadotropin was less than 1.2mIU/ml. Computed tomography (CT) scan revealed a mass in the retroperitoneum within the para-aortic region (Fig 1).

The patient underwent laparotomy and excision of the retroperitoneal mass. Gross inspection of the mass resembled an enlarged para-aortic lymph node which was situated on the left side of the retroperitoneum. No other lymphadenopathy was present elsewhere. Macroscopic examination revealed a lobulated firm mass measuring 5.5 X 3.5 X 3.0 cm. Cut section showed a solid homogenous greyish area with areas of necrosis. Microscopically, the mass composed of lymphoid tissue extensively replaced by malignant cells. Immunohistochemistry studies showed that the

tumour cells were positive for alpha-feto protein. Thus it was concluded that this lymph node represented a metastatic mixed germ cell tumour (yolk sac and embryonal carcinoma).

Ultrasound revealed normal echo pattern of bilateral testis. No focal lesions were seen. The right testis measured 2.6 X 3.6, while left testis measured 2.8 X 3.6cm. With the diagnosis of extra-gonadal germ cell tumour, the patient underwent 4 cycles of chemotherapy with each 3-week cycle consisting of bleomycin, cisplatin, and etoposide. Five months following chemotherapy CT abdomen revealed no residual tumour. The alpha-feto protein levels reduced on follow up (from 263 to 5.8ng/ml). He was counselled for a testicular biopsy but opted for regular surveillance instead. He remains tumour free 12 months after diagnosis.



Fig 1: CT abdomen of left para-aortic mass (arrow).

Discussion

Extra-gonadal germ cell tumours (EGGCT) are a rare entity. It represents 5-10% of all germ cell tumours (1). They have a predilection to occur along midline structures such as the retroperitoneum, pineal gland and mediastinum. True EGGCT are difficult to ascertain unless we exclude a primary source from the testis. An assumed EGGCT may actually represent a metastatic tumour from an indolent or clinically undetected primary germ cell tumour of the testis.

There are two possible reasons for this occurrence. In one situation, the testis may harbour an occult tumour that has metastasized but it is normal on clinical examination. However an ultrasound examination may reveal a small testicular lesion. This would then

be confirmed by a testicular biopsy or an orchidectomy (2).

Secondly, the retroperitoneum may represent metastases from a testicular primary which has regressed, the so called "Burnt-Out" phenomenon. Here, clinical and ultrasonography of the testis will be normal. An orchidectomy or biopsy, if performed, or may demonstrate areas of scarring as the primary tumour undergoes necrosis (2).

Daugaard et al (1987) in his series of 15 EGGCT patients, found evidence of testicular intraepithelial neoplasia in 42% and carcinoma in situ in 53% of patients (3). All 15 patients were without clinical signs of a testicular tumour. In addition, 3 of these patients had small areas of invasive tumour growth. He concluded that germ-cell tumours can only be diagnosed as extragonadal in origin if testicular biopsy shows no malignant features or scarring. In a separate review of 14 patients with apparent EGGCT who underwent orchidectomy after chemotherapy, 71% had histological evidence of a testicular primary (20% teratoma, 80% focal necrosis or fibrosis). This was especially true if their retroperitoneal metastases were only unilateral, which corresponds to an ipsilateral testicular primary (4).

Metachronous testicular malignancies do occur. In one series of 635 patients with apparent EGGCT, the rate of metachronous lesions was 4.1% with a cumulative risk 10 years after diagnosis being 14.2%. This was seen in patients with non-seminomatous retroperitoneal EGGCT (5).

There are reports of the development of testicular recurrence as high as 31%, even after systemic response to primary chemotherapy (5). Leibovitch *et al* (1996) in a retrospective analysis of the orchidectomy specimens of 160 patients with metastatic non-seminomatous germ cell tumors who underwent delayed orchidectomy and retroperitoneal lymph node dissection post chemotherapy revealed necrosis or scar in 70 (43.7%), pure teratoma in 50 (31.2%) and persistent germ cell cancer in 40 (25%). They concluded a need for delayed orchidectomy even after a partial or complete response to systemic chemotherapy (6.) This phenomenon may be explained by the existence of blood testis barriers and tumor heterogeneity. Our patient underwent 4 cycles of chemotherapy with no evidence of residual tumour based on imaging of the abdomen and normalization of the alpha-feto protein on follow up.

Based on the evidence so far however, he was advised for either a testicular biopsy rule out presence of an occult primary or a burnt out testicular lesion. If such

a lesion was present, then an orchidectomy would follow. This would help prevent the occurrence of a delayed testicular recurrence in the near future. Additionally, current evidence points that the best chance of detecting a positive finding in a testis is if the retroperitoneal mass was unilateral, as it was in our patient. However our patient refused any surgical intervention. There has been no local or distant recurrence past one year. He is now on three monthly testicular examination, ultrasound examination and alpha-feto protein levels. As there are no standard protocols available for follow up, a reasonable surveillance protocol would be to follow up 3 monthly for the first 2 years and then once a year for as long as ten years. The patient should also be advised to perform a self testicular examination regularly and consult the attending surgeon immediately if any abnormality is detected.

Conclusion

There will always be an on-going debate regarding the true existence of an extra-gonadal germ cell tumour. Current evidence from testicular biopsies and orchidectomies for extra-gonadal germ cell tumour reveal a 40-50% change of detecting a primary testicular lesion, therefore prompting physicians to advocate testicular biopsy all cases (3). In patients who elect not to, they should be counselled regarding the presence of harbouring a clinically occult tumour and the possibility of a testicular recurrence despite systemic chemotherapy. In such a situation, an active surveillance protocol comprising of testicular examination, ultra-sonography and check of tumour marker levels are necessary. The patient should also be followed up for a minimum of ten years.

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